

*What Is Claimed Is:*

1. A method for inhibiting the biological response of a eukaryotic cell to a cytokine, comprising
  - (A) inhibiting the activity of a Jak kinase in said eukaryotic cell, wherein said response is mediated by the activation of said Jak kinase, and wherein, when said Jak kinase is Jak2, said cytokine is other than erythropoietin (EPO) or interleukin-3 (IL-3).
2. A method according to claim 1, wherein said cytokine elicits said biological response by binding a tyrosine kinase receptor.
3. A method according to claim 1, wherein said cytokine elicits said biological response by binding to a cytokine receptor.
4. A method according to claim 1, wherein said Jak kinase is selected from the group consisting of Jak1, Jak2, Jak3, and Tyk2.
5. A method according to claim 1, wherein said cytokine is selected from the group consisting of interleukin-3 (IL-3), granulocyte-macrophage specific colony stimulating factor (GM-CSF), erythropoietin (EPO), granulocyte colony stimulating factor (G-CSF), interferon- $\gamma$  (IFN- $\gamma$ ), prolactin hormone, and growth hormone.
6. A method according to claim 1, wherein said cytokine is selected from the group consisting of interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 5 (IL-5), interleukin 6 (IL-6), interleukin 7 (IL-7), interleukin 9 (IL-9), interleukin 11 (IL-11), interleukin 6 (IL-6), oncostatin M (OSM), leukemia inhibitory factor (LIF), and an interferon.
7. A method according to claim 1, wherein the activity of said Jak kinase is inhibited by introducing into said eukaryotic cell effective amounts of a composition capable of inhibiting the expression of said Jak kinase in said eukaryotic cell.
8. A method according to claim 7, wherein said composition is selected from the group consisting of an antisense and a ribozyme.

9. A method according to claim 1, wherein the activity of said Jak kinase is inhibited by introducing into said eukaryotic cell effective amounts of a composition capable of inhibiting said activity.

5 10. A method according to claim 9, wherein said composition is selected from the group consisting of an antibody against said Jak kinase, an antagonist to said Jak kinase, a *trans*-dominant mutant of said Jak kinase, and a peptide fragment of said Jak kinase.

10 11. A method according to claim 1, wherein the activity of said Jak kinase is inhibited by introducing into said eukaryotic cell effective amounts of a composition capable of inhibiting the activation of said Jak kinase.

15 12. A method according to claim 11, wherein said composition is selected from the group consisting of an antibody against said Jak kinase, an antagonist to said Jak kinase, a *trans*-dominant mutant of said Jak kinase, and a peptide fragment of said Jak kinase.

20 13. A method for treating a disease condition in an animal caused by an excessive response of cells in said animal to a cytokine whose activity is mediated by the activation of a Jak kinase, the method comprising

(A) inhibiting the activity of said Jak kinase in said cells, wherein, when said Jak kinase is Jak2, said cytokine is other than erythropoietin (EPO) or interleukin-3 (IL-3).

25 14. A method according to claim 13, wherein said disease condition is an excessive proliferation of said cells.

30 15. A method for treating a deficient response of a eukaryotic cell to a cytokine other than interferon- $\alpha$  (IFN $\alpha$ ) whose activity is mediated by the activation of a Jak kinase comprising increasing the level of Jak kinase in said eukaryotic cell, wherein said deficient response is due to the presence of abnormally low levels of the activated form of said Jak kinase in said eukaryotic cell after contact with said cytokine, and wherein, when said Jak kinase is Jak2, said cytokine is other than erythropoietin (EPO) or interleukin-3 (IL-3).

16. A method according to claim 15, wherein the level of said Jak kinase in said eukaryotic cell is increased by enhancing the expression of Jak kinase in said eukaryotic cell.

5 17. A method according to claim 16, wherein the expression of said Jak kinase is enhanced by introducing a vector capable of expressing said Jak kinase in said eukaryotic cell.

10 18. An assay for identifying a composition capable of inhibiting the biological response of a eukaryotic cell to a cytokine whose activity is mediated by the activation of a Jak kinase comprising detecting the ability of said composition to inhibit the *in vitro* kinase activity of said Jak kinase, wherein, when said Jak kinase is Jak2, said cytokine is other than erythropoietin (EPO) or interleukin-3 (IL-3).

15 19. The assay of claim 18, comprising

(a) preparing a first reaction mixture comprising said Jak kinase in activated form, a substrate for said Jak kinase, and adenosine triphosphate (ATP) with a detectably labelled phosphorous at the  $\gamma$  position, all combined in a kinase buffer;

20 (b) preparing a second reaction mixture comprising said first reaction mixture combined with said composition; and

25 (c) detecting said substrate containing said detectably labelled phosphorous in said first and said second reaction mixture;

wherein said composition is identified as capable of inhibiting the biological response of a eukaryotic cell to a cytokine whose activity is mediated by the activation of said Jak kinase if said second reaction mixture contains significantly less amounts of said substrate containing said detectably labelled phosphorous than said first reaction mixture.

20. The assay of claim 19, wherein said substrate is said Jak kinase or a fragment thereof comprising the autophosphorylation site of said Jak kinase.

21. The assay of claim 20, wherein said Jak kinase comprises an amino acid sequence corresponding to amino acids 1000-1015 of SEQ ID NO:2.

22. An assay for identifying a composition capable of inhibiting the biological response of a eukaryotic cell to a cytokine whose activity is mediated by the activation of a Jak kinase comprising detecting the ability of said composition to inhibit said activation.

23. The assay of claim 22, comprising the steps of:

(a) preparing as first extract from a first population of said eukaryotic cell after stimulation with said cytokine, said extract comprising said Jak kinase and a substrate for said Jak kinase;

(b) preparing a second extract from a second population of said eukaryotic cell after stimulation with said cytokine, said extract comprising said Jak kinase and a substrate for said Jak kinase, wherein said composition is provided to said second population before or during said stimulation;

(c) preparing a first reaction mixture comprising said first extract combined with adenosine triphosphate (ATP) with a detectably labelled phosphorous at the  $\gamma$  position in a kinase buffer;

(d) preparing a second reaction mixture comprising said second extract combined with adenosine triphosphate (ATP) with a detectably labelled phosphorous at the  $\gamma$  position in a kinase buffer; and

(e) detecting said substrate containing said detectably labelled phosphorous in said first and said second reaction mixture;

wherein said composition is identified as capable of inhibiting the biological response of a eukaryotic cell to a cytokine whose activity is mediated by the activation of said Jak kinase if said second reaction mixture contains significantly less amounts of said substrate containing said detectably labelled phosphorous than said first reaction mixture.

24. An assay for identifying a composition capable of inhibiting the biological response of a eukaryotic cell to a cytokine whose activity is mediated by the activation of a Jak kinase comprising detecting the ability of

said composition to inhibit, in the presence of said cytokine, the physical interaction between said Jak kinase and the receptor for said cytokine.

25. An antibody which selectively binds an epitope of a peptide having a sequence substantially corresponding to a member selected from the group consisting of amino acids 786-804 of Jak1 (SEQ ID No. 6), amino acids 758-776 of Jak2 (SEQ ID No. 5), and amino acids 819-837 of Tyk2 (SEQ ID No. 7), wherein said antibody is capable of specifically binding to the Jak kinase from which said peptide is derived without interfering with the activity of said Jak kinase.

26. ~~27~~ An isolated DNA molecule comprising a DNA sequence encoding a Jak kinase capable of undergoing tyrosine phosphorylation by at least one cytokine.

~~27. ~~28~~ An isolated DNA molecule according to claim 27, comprising a DNA sequence corresponding to a portion of SEQ ID NO:2.~~

28. ~~29~~ An isolated DNA molecule according to claim 27, comprising a DNA sequence corresponding to a portion of Figure 6 (SEQ ID NO:).

29. ~~30~~ An isolated DNA molecule according to claim 27, wherein said DNA sequence is derived from the murine Jak2 gene sequence as shown in Figure 1 (SEQ ID No. 8).

30. ~~31~~ An expression vector, comprising the isolated DNA molecule of claim 27, said vector capable of expressing said Jak kinase in a host.

31. ~~32~~ A host transformed with the expression vector of claim 31.

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